REMARKS

Claim Amendments

The present amendments and claim cancellations are made without prejudice to presenting any of the deleted and/or cancelled subject matter in one or more continuing applications.

Claim 1 is amended such that the preamble now recites, "[a] method of 'detecting whether a patient has asymptomatic coronary artery disease in which' a sample taken from a human patient who is asymptomatic for coronary artery disease 'is analyzed' for factors associated with coronary artery disease." Claim 1 is also amended such that step (c) begins with the recitation, "'detecting' whether the patient has 'asymptomatic' coronary artery disease..." Support for these amendments is found throughout the specification, for example, in the Title; at page 21, lines 8-10, page 15, lines 21-22; page 11, lines 17 to page 13, line 2; page 47, lines 3-12; and original claim 1. Although the word "detecting" was not mentioned during the Interview, use of the word is well supported and appropriate in these claim amendments.

Claim 22 step (d) is amended to recite "providing to the medical professional the appropriate one or more of the cut-points 'for' the medical professional to 'determine' whether the patient has 'asymptomatic' coronary artery disease..." The amendments are supported throughout the specification, for example, at page 31, line 27 to page 32, line 10, particularly page 32, line 2; page 14, lines 12-14; the Title; page 21, lines 8-10, page 15, lines 21-22; page 47, lines 3-12; and original claim 22.

Claims 1 and 22 are each amended to replace "based on" with "for" where referencing a particular cut-point or particular value for one or more recited factors,

such as atherogenic protein, acute phase reactant, and/or anti-atherogenic protein. Support is found throughout the specification whether from explicit, implicit, or inherent disclosure, for example, at page 27, lines 23-24; page 23, line 29 to page 25, line 5 including Table I on page 25 lines 1-5; and page 29, lines 5 to page 31, line 19.

Claim 1 has been amended to incorporate the subject matter of claims 9 and 11 at the end of step (a). Also, claim 22 has been amended to incorporate the subject matter of claims 30 and 32 at the end of step (a). Each of claims 1 and 22 has thus been amended to recite at the end of step (a) that "at least one of the following monoclonal antibodies is used in an immunological assay to obtain the level of atherogenic protein: mAb-4E6 produced by hybridoma Hyb4E6 deposited with the BCCM (Belgian Coordinated Collections of Microorganisms) under deposit accession number LMBP 1660 CB, mAb-1H11 produced by hybridoma Hyb1H11 deposited with the BCCM under deposit accession number LMBP 1659 CB, and mAb-8A2 produced by hybridoma". Support is provided throughout the specification, particularly at page 15, lines 8 and 10-17; and in original claims 9 and 11.

Claims 9, 11 and 21 have been cancelled and claims 12 and 13 have been amended because the amendments to claim 1 incorporating the subject matter of claims 9 and 11 has rendered the subject matter of the cancelled claims and deleted portions of claims 12 and 13 redundant.

Similarly, claims 30, 32 and 42 have been cancelled and claims 33 and 34 have been amended because the amendments to claim 22 incorporating the subject matter of claims 30 and 32 has rendered the subject matter of the cancelled claims and deleted portions of claims 33 and 34 redundant.

Interview Summary

Applicants thank Primary Examiner David Venci and Supervisory Examiner Long Le for the courtesies extended to the undersigned during the telephonic Interview that was held on March 11, 2008. The outstanding request for Examiner consideration and sign-off of review of references cited by Applicants in the various Information Disclosure Statements was discussed. The Examiners stated that Applicants need not resubmit the Information Disclosure Statements. Examiner Venci indicated that the acknowledgment of review will be included with the next issued Action.

Also during the Interview, the outstanding rejections were discussed and various proposals for amendments to the claims were made by the undersigned. No objections were made by the Examiners to any of these proposals.

Examiner Le also suggested incorporating into the independent claims an assay parameter, particularly the subject matter of claim 11, which recites monoclonal antibodies for use in an immunological assay to obtain the level of atherogenic protein.

35 USC 101

A. Statutory Subject Matter

Claims 22-30, 32-34 and 36-42 were rejected under 35 USC § 101 as directed to non-statutory subject matter. (Paper No. 20070831 at 2.) Although the

Examiner did not list claim 1 as being rejected under this basis, the Examiner addressed claims 1 and 22 directly following the rejection.

Applicants submit that a rejection was not properly made under this basis for claim 1 and that therefore the rejection does not apply to claim 1. In the interests of furthering prosecution, however, Applicants include comments pertaining to claim 1.

In making the rejection, the Examiner stated that "claims 1 and 22 do not require ... patient 'samples' [and the] Examiner interprets the verbiage in claims 1 and 22 as non-statutory 'abstract ideas'..." (Id.)

As indicated during the Interview, a "sample" from a patient is recited in the claims and the claim term represents something tangible. Claims 1 and 22, step (a), for example, recite "obtaining the level of an atherogenic protein in a ***sample*** from the patient, obtaining the level of an acute phase reactant in a ***sample*** from the patient, and optionally obtaining the level of an anti-atherogenic protein in a ***sample*** from the patient". The specification provides disclosure regarding a "sample" on page 26, line 29 through page 27, line 21. Particularly, the specification discloses that "[t]he one or more samples may comprise solid, liquid, and/or gas. For example, samples may comprise tissue or fractions or derivatives thereof (e.g., tissue extract) or whole blood or other body fluids or fractions or derivatives thereof (e.g., plasma, serum)." Page 27, lines 3-6. Clearly, a "sample" from a patient is not an "abstract idea", as contended by the Examiner.

It is submitted that the rejection under section 101 asserting non-statutory subject matter has been overcome. Reconsideration and withdrawal of the rejection are requested.

B. Credible Utility

Claims 1-9, 11-13, 15-30, 32-34 and 36-42 were rejected under 35 USC § 101 as lacking credible utility. (Id. at 3) In making the rejection, the Examiner refers to claims 1 and 22 as "[requiring], *inter alia*, patients having an 'asymptomatic disease' (i.e., asymptomatic coronary artery disease)." The Examiner asserted that this "creates a semantic construct wherein a person simultaneously has a disease, yet is asymptomatic for that disease." (Id.) The Examiner further asserted that "Applicant's assertion of utility is premised on data obtained from a clinical study ... involving two semantic classes of individuals" which are healthy (controls) and not healthy (diseased). (Id.) The Examiner asserted that the "specification does not disclose any semantic class of individuals who are simultaneously healthy and not healthy..." (Id. at 4)

As discussed during the Interview, it is pointed out that the preambles of claims 1 and 22 recite "a sample ... from ***a human patient who is asymptomatic for coronary artery disease***". The sample tested is thus from a patient who is asymptomatic for CAD. Such a patient may have CAD but be asymptomatic, or such a patient may not have CAD, i.e., be healthy as to this parameter. This population is clearly disclosed throughout the specification as, for example, page 15, lines 21-22, as those who are asymptomatic but who can benefit from the claimed methods with regard to "significantly better discrimination between those who have [CAD] and those who do not but all of whom are asymptomatic."

The claimed methods provide for testing of such asymptomatic patients in order to determine, for example, ***whether a patient has asymptomatic coronary***

artery disease", and therefore has the disease. Such language is found, for example, in amended claim 1, preamble lines 1-2 and step (c) lines 1-2, and in claim 22, the preamble, lines 3-4, and step (d) lines 2-3. Contrary to the Examiner's assertion, the patient population of those who have asymptomatic CAD is disclosed throughout the specification. Support includes, for example, the Title of the application, page 47, lines 8-13, page 11, lines 18-19, page 13, lines 4-5, page 15, lines 21-22.

Applicants submit that the application provides support for the assertion of utility throughout the specification. And, contrary to the Examiner's contention, the clinical data analysis provided in the specification supports the asserted utility. See, for example, Table IV on page 44 in which values for the control, stable (chronic) angina population and the acute coronary syndromes population are provided. The specification discloses that "[a]s will be understood by one skilled in the art, broadly speaking, for two given distributions, (e.g., one distribution or curve of negatives and the other of positives), if the means of two distributions are farther apart (all else being equal), there will tend to be less overlap of the two distributions. Page 44, line 4 to Page 45, line 2. In comparing the distributions, for example, between the control group and "the Stable (Chronic) Angina sub-population", the specification discloses that the results "[indicate] a good separation between means and, therefore, less overlap." Page 45, lines 3-7. Furthermore, the advantage over control is provided in Table IV for the stable (chronic) angina population and the acute coronary syndromes population. The calculated advantage for (i) OxLDL x CRP, and (ii) OxLDL x CRP/HDL of the present invention are significantly greater than comparison groups (a) to (e). See also Page 47, lines 3-20.

Furthermore, as was noted during the Interview, page 44, lines 1-6 of the specification, a portion of which was referenced by the Examiner in the Action, indicates that although the control group of individuals is assumed to be "true negatives", the specification also discloses that "this is believed to be a conservative assumption because some of the control individuals, all of whom are asymptomatic, may in fact have [CAD]". Page 44, lines 4-6. The finding of good statistical separation between the "conservative" control group and diseased populations thus further supports the utility of the claimed invention rather than the converse.

Also contrary to the Examiner's contention, a defined clinical study group having asymptomatic CAD is not required to establish utility in the present case. The claims under consideration are not directed to a method of treatment. And, as noted above, the clinical data analysis actually supports the utility asserted.

35 USC 112, First Paragraph

Claims 1-9, 11-13, 15-30, 32-34 and 36-42 were rejected under 35 USC § 112, first paragraph. (Id. at 5) In making the rejection, the Examiner asserted that "since the claimed invention is not supported by either a credibly asserted utility or a well established utility for the reasons set forth above, one skilled in the art ... would not know how to use the claimed invention." (Id.)

Applicants incorporate the arguments presented above in response to the 35 USC § 101 rejection as allegedly lacking utility. Credible utility for the asserted utility

in the specification is clearly present. Accordingly, the rejection has been rendered moot and should be withdrawn.

Furthermore, the Examiner has not indicated what aspect of the claims one skilled in the art allegedly would not know how to use. It is submitted, therefore, that the rejection is deficient and for this reason alone, should be withdrawn.

35 USC § 112, Second Paragraph

Claims 1-9, 11-13, 15-30, 32-34 and 36-42 were rejected under 35 USC § 112, second paragraph, as being indefinite. (Id. at 6)

"In rejecting a claim under the second paragraph of section 112, ***it is incumbent on the Examiner to establish that one having ordinary skill in the art would not have been able to*** ascertain the scope of protection defined by the claim when read in light of the supporting specification." *Ex parte Cordova*, 10 USPQ2d 1949, 1952 (Board of Pat. App. and Int. 1989), citing *In re Moore*, 169 USPQ 236 (CCPA 1971).

For the various bases for this rejection, the Examiner has failed to provide any reason to support the assertion that one skilled in the art would not understand the scope of the present claims, when viewed in light of the specification. For this reason, the rejection must be withdrawn.

In making the rejection, the Examiner first asserted that "[t]he preamble of claim 1 does not correspond to the method outcome." (Id.)

Applicants have amended the preamble of claim 1 such that it recites, "[a] method of detecting whether a patient has asymptomatic coronary artery disease in

which a sample taken from a human patient who is asymptomatic for coronary artery disease is analyzed for factors associated with coronary artery disease." It is submitted that the amendment renders the rejection moot.

The Examiner also asserted that "[i]n claims 1 and 22, the various sections of step (b), the phrase 'based on' is indefinite.... The identity of one or more objects and/or steps required for 'basing' or 'relating' an abstract variable (*i.e.*, a 'cut-point') using an inanimate noun (*e.g.*, an 'acute phase reactant) is not clear." (Id.)

Applicants have amended the claims to replace the term "based on" with the word "for". It is submitted that the amendments obviate this rejection.

Applicants also note that the specification clearly states that "[a] cut-point (or threshold value) is a value for a given parameter (e.g., analyte) that divides a positive indication from a negative indication." Page 27, line 23-24. Further information pertaining to cut-points is found in the specification, for example, at page 24, line 10 though page 25, line 5 (Table I); page 26, lines 12-15 and lines 22-28; page 27, lines 22 to page 29, line 4; page 30, lines 8-12. It is submitted that one skilled in the art would understand the meaning of a first, second, etc. cut-point for one or more factors as recited, i.e., atherogenic protein, acute phase reactant, and/or anti-atherogenic protein, when read in light of the specification.

The Examiner further asserted that in claim 1, the various sections of step (c), "[t]he identity of two or more parameters subject to 'comparison' is not clear. Whether/how 'the level of the atherogenic protein' obtained in step (a) provides basis for 'first value' is not clear." (Id. at 6-10)

We note that disclosure pertaining to the first, second, etc., values is found in the specification, for example, from page 23, line 29 through page 25, line 5, which includes Table I on page 25, and page 29, line 5 to page 31, line 19. As indicated to the Examiners during the Interview, the first, second, etc. values are understood upon viewing Table I on page 25. For example, under column (i), the level of atherogenic protein and the level of acute phase reactant are each used separately to provide a first value for the level of the atherogenic protein and a second value for the level of the acute phase reactant. (Total values listed under the heading "Total values and total cut-points each needed" for column (i) are 2.) In another example, under column (ii), the levels of atherogenic protein and acute phase reactant are used together to provide a third value for the levels of atherogenic protein and acute phase reactant. (Total values listed under the heading "Total values and total cut-points each needed" for column (ii) is/are 1.) The specification discloses that "the levels obtained for a patient may be mathematically manipulated alone or in groups of two..." Page 30, lines 16-17. Where two levels are used together, the specification discloses, for example, that "the atherogenic protein level for a patient [is] multiplied by the acute phase reactant level for that patient, thereby to obtain a single value that is related to the levels of atherogenic protein and acute phase reactant..." Page 30, lines 17-19. One skilled in the art would understand the meaning of a first, second, etc., value for a given one or more factors when read in light of the specification.

It is submitted that the identity of parameters subject to comparison is sufficiently clear. It is also submitted that the manner in which the levels obtained in

step (a) provide a first, second, etc., value is also sufficiently clear under 35 USC § 112. Withdrawal of the rejection is requested.

The Examiner further asserted that "[t]he preamble of claim 22 does not correspond to the method outcome. The Examiner contended that "the preamble of claim 22 recites a method for providing 'a sample' information, while step (d) ... merely requires a step of providing 'cut-point' information'.... One or more steps of providing 'a sample' information appears to be omitted from claim 22." (Id. at 10)

It is pointed out that step (c) recites "providing to the medical professional at least one of" a first, second, etc. value, where each value is for one or more factors as recited, i.e., atherogenic protein, acute phase reactant, and/or anti-atherogenic protein. The relationship between the values and the levels of one or more factors is disclosed in the specification, and it is discussed above. The Examiner has ignored step (c), yet the preamble language of providing a sample information referenced by the Examiner is supported by the claim, including step (c).

It is submitted that the preamble and the recited steps supporting the language of the preamble are sufficiently definite. Withdrawal of the rejection is requested.

With regard to claim 22, the various sections of step (c), the Examiner contended that the phrase 'based on' is indefinite.... The identity of one or more objects and/or steps required for 'basing' or 'relating' an abstract variable (*i.e.*, a 'first value') using a protein level (*e.g.*, the level of the atherogenic protein) is not clear." (Id. at 10-13)

Applicants have amended claim 22, section (c), to replace the term "based on" with the word "for". It is submitted that the claim amendment obviates this rejection.

Furthermore, Applicants refer the Examiner to the remarks above concerning use of the terms first, second, etc., values including reference to the specification. It is submitted that one skilled in the art would understand the meaning of the first, second, etc., value terms used in claim 22, section (c) when read in light of the specification.

It is submitted that this rejection has been rendered moot and should be withdrawn.

Finally, the Examiner asserted that "[i]n claim 22, step (d), the infinitives 'to permit' and 'to assess' are indefinite." (Id. at 13)

Applicants have amended claim 22 step (d) to recite "providing to the medical professional the appropriate one or more of the cut-points 'for' the medical professional to 'determine' whether the patient has 'asymptomatic' coronary artery disease...". It is submitted that the amendments obviate the rejection, and withdrawal of the rejection is requested.

It is further submitted that all of the bases for rejection under 35 USC § 112, second paragraph, have been rendered moot.

Furthermore, Applicants have made the amendments to claims 1 and 22 noted above as suggested by Examiner Le in the Interview.

For the reasons set forth above, it is submitted that the application is in condition for allowance. Withdrawal of the rejections and allowance of the claims are

respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on March 17, 2008.

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Respectfully submitted,

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